Assessment of validation of health-economics decision models in intervention studies of seasonal influenza and breast cancer

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Of 630 articles identified, four studies passed the inclusion criteria, and three were included by searching reference lists. Subsequently, we add more than 150 conference papers to the screening three-step procedure. **CONCLUSIONS:** The use of modelling is promising in this context. It can be explained by the required features of any early cost-effectiveness evaluation seeking to inform decision making. We aimed at distinguishing from the previous works, addressing this methodology. It should be stressed the very small amount of the papers on the topic. In addition, we highlight the absence of ad-hoc checklist and coding to be used for the quality assessment of early model-based analyses and data extracted classification. This work also tries to advance in the definition of appropriate criteria to evaluate the reliability of the analysis in terms of impact on primary stakeholders.

PRM121

ASSESSMENT OF VALIDATION OF HEALTH-ECONOMICS DECISION MODELS IN INTERVENTION STUDIES OF SEASONAL INFLUENZA AND BREAST CANCER

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OBJECTIVES: We aimed to review recently published health-economic (HE) decision models to assess the reporting of validation efforts. An infectious disease (seasonal influenza, SI) and a chronic disease (breast cancer, BC) were used as examples, giving a preliminary insight in the reporting of validation efforts in the overall HE literature. **METHODS:** A literature search was performed in Pubmed and Embase to retrieve full-text HE modeling studies, published between 2008 and 2014. Type of evaluation, model and intervention were extracted, as well as information on model outcomes, journal and funding. Reporting on model validation was evaluated by checking for the presence of the word validation and its conjugates, and by using AdViSHE, a tool which contains a structured list of relevant items for validation. **RESULTS:** The literature search resulted in 53 SI and 45 BC studies. In 41 studies (42%) the word validation or its conjugates was mentioned, but only in a small percentage in the context of model validation. The terminology used around validation was found to be ambiguous. Model validation efforts were reported in a minority of studies. However, some studies do show good reporting examples. Cross validation of study outcomes was reported most often, but the quantity and quality of this reporting varied. More validation efforts were reported in BC than in SI. **CONCLUSIONS:** Only a limited number of studies reported on model validation efforts, although it may be assumed that more efforts have been taken than were reported. In particular, the differences between SI and BC may not mean that less efforts were undertaken to validate SI models. Although validation is deemed important by many researchers, this is not reflected in the reporting habits of HE modeling studies. Better reporting of validation efforts would be desirable to further enhance decision-makers' confidence in HE models and their outcomes.

PRM122

SENSITIVITY ANALYSIS: HOW MUCH IMPACT DOES IT HAVE ON THE NICE DECISION MAKING PROCESS?

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OBJECTIVES: As part of economic evaluations submitted to NICE, probabilistic and deterministic sensitivity analysis are a requirement, with probabilistic sensitivity analysis being a stated preference in the NICE reference case. The aim of including sensitivity analysis is to identify the key areas of uncertainty, and determine the impact on results. The aim of this analysis was to assess what impact uncertainty in cost-effectiveness models has had on NICE reimbursement decisions and review what type of sensitivity analyses are conducted. **METHODS:** The five most recent NICE appraisals for breast cancer were selected, the sensitivity analysis results and methods were extracted. Once extracted the results of the sensitivity analysis were compared and contrasted. The sensitivity analysis results were considered in the context of the base case results. **RESULTS:** The methodology of sensitivity analysis conducted varied between submissions, whilst all appraisals conducted univariate sensitivity analysis only two reported tornado diagrams. The method of reporting results also varied between appraisals, of the four appraisals that had more than one comparator in the base case, only one appraisal conducted a multiway cost-effectiveness acceptability analysis. **CONCLUSIONS:** There are many factors that impact a NICE committees decision, therefore it is not possible to draw a conclusion on how the uncertainty impacted the decision making process. Of the appraisals assessed, there was a wide range of differences between deterministic and probabilistic ICERs, however it appears that this did not impact the appraisal. The sensitivity analysis reported across NICE submissions lacks consistency in the observed sample, hindering the comparison between submissions.

PRM123

HOW TO MODEL SURVIVAL IN COST-EFFECTIVENESS ANALYSIS? DIFFERENCES BETWEEN MARKOV AND PARTITIONED SURVIVAL ANALYSIS MODELS

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OBJECTIVES: The choice of a modeling approach is guided by key criteria including time, interaction between individuals, and the unit of analysis (cohort or individuals level models). Despite Markov cohort modeling (MCM) is widely used in the literature, the use of partitioned survival (PS) models tends to increase. Our objective is to explore the rationale for selecting either a Markov modeling approach or a PS approach to carry-out a cost-effectiveness analysis in oncology. Our study focuses on the differences between the two approaches. **METHODS:** A literature review focusing on survival modeling in economic evaluation was performed in order to establish a list of differences between the two modeling approaches. Besides, we reviewed NICE's technology appraisals (TA) in oncology medicines over the last two years (2013-2015) to analyze the practices and the arguments put forward to justify modeling choices. Data collected for each TA included: model type, rationale for model selection, health states, hypotheses, survival analysis, clinical data sources and the treatment of uncertainty. **RESULTS:** Twelve economic evaluations in oncology were submitted to NICE by pharmaceuticals companies (PC) between 2013 and 2015. Seven PC submitted a MCM, two a PSM, two a semi-markov partitioned survival model, and one a semi-markov model (SMM). Differences between modeling techniques were classified into four items: clinical data sources (e.g. published aggregated data for MCM and limited IPD for PSM), structure (e.g calculation of transition probabilities for MCM), hypotheses (e.g. same transition probability of death between two health states for MCM), flexibility of the model (e.g. access to patient level data for comparators required in PSM). **CONCLUSIONS:** Being a more flexible modeling technique, Markov models remain more frequently used compared to PSM. Nevertheless, PSM represent a more straightforward option when patient level data are available but are inappropriate when such data are not accessible for comparators.

PRM124

PHYSICIANS' CHOICE AS A COMPARATOR IN CLINICAL TRIALS: CHALLENGES FOR PHARMACOECONOMIC MODELLING OF INNOVATIVE TREATMENTS TO SUPPORT HEALTH TECHNOLOGY ASSESSMENTS

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OBJECTIVES: To identify specific challenges for modelling to support health technology assessment (HTA) submissions using trial data where the comparator is the physician's choice (PC). **METHODS:** Most clinical trials are designed globally or internationally, with minimal consideration of individual market needs. It is increasingly common for investigational drugs to be compared against a mix of PC treatments because a standard of care (SOC) is not always clearly defined. We searched a clinical trials database for registered trials where PC was the comparator. Based on the standard requirements for pharmacoeconomic models to support HTAs, we evaluated trial information to identify specific modelling challenges. **RESULTS:** We found 49 registered trials using PC as the comparator and identified four specific challenges that require guidance from HTA bodies. (1) One or more drugs used in PC regimens may not be licensed for an individual market, rendering their use problematical. (2) Comparison made against individual PC drugs results in lower patient numbers for comparison, reducing analysis credibility. (3) Analysis against individual PC drugs requires breaking randomisation, which jeopardises trial design integrity. (4) Involvement of a PC mix results in the need for a full incremental analysis, which might lead to application rejections in circumstances where the new treatment may only have incremental benefits over some of the individual treatments. **CONCLUSIONS:** The use of PC as a comparator in clinical trials poses challenges that are likely to slow the process of access to effective, innovative treatments. HTA agency involvement early in the life cycle of a technology would facilitate a shared understanding of evidence requirements. HTA agencies should develop clear guidelines on how PC efficacy and cost should be used for pharmacoeconomic modelling.

PRM125

EVALUATION OF THE EFFECT OF CRUDE LEAVES EXTRACT OF INDIGOFERA SPICATA FORSSK.(FABACEAE) ON BLOOD GLUCOSE LEVEL OF NORMOGLYCEMIC, ORAL GLUCOSE LOADED AND ALLOXAN INDUCED DIABETIC RODENTS

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OBJECTIVES: to evaluate the effect of the hydro-alcoholic leaves crude extract of Indigofera spicata(ISP) on the blood glucose level(BGL) of normoglycemic, oral glucose loaded and alloxan induced diabetic rodents. **METHODS:** The animals were randomly divided into five groups (n=6) for all the aforementioned three models. In all models, group-I mice provided 2%tween-80, group-II were treated with 5mg/kg glibenclamide and the remaining three groups(III, IV &V) were treated with 100, 200, and 400mg/kg dose of the extract respectively. Statistical significance of differences in BGLs within and between groups was analyzed by SPSS version-21 using one way ANOVA followed by Tukey's post hoc multiple comparison. **RESULTS:** 200mg/kg and 400mg/kg extract treated groups of normoglycemic mice showed significant ($p<0.05$) BGL reduction compared to the pre-exposure level. In case of OGTT model BGL reduction was statistically significant ($p<0.05$) in only 400mg/kg exposed groups at the 120 minute of post-exposure compared to the initial level. However, the BGL reducing effect of doses of the extract at the 4th, 6th and 10thhours of post treatment on diabetic mice was found statistically significant compared to both the negative control($p<0.001$) and their respective pretreatment levels($p<0.05$). **CONCLUSIONS:** Generally the crude extract of ISP leaves have shown prominent anti-diabetic effect and can be therefore used as a good insight for novel anti-diabetic drug discovery and development with a call of further in vitro and in vivo studies.

PRM126

DISEASE PROGRESSION IN RHEUMATOID ARTHRITIS: KEY ELEMENT FOR COST-EFFECTIVENESS MODELLING

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OBJECTIVES: To identify and assess disease progression models used in rheumatoid arthritis (RA) cost-effectiveness modelling. **METHODS:** We examined all studies identified in two recent systematic literature reviews on health economic decision models evaluating RA treatments. We identified the elements in these studies describing disease progression and classified them by outcome measure affected and by model type. **RESULTS:** Disease progression models concern in most cases the health assessment questionnaire (HAQ) score. The reported individual sampling models and discrete event simulation models make assumptions about improvement of the HAQ when treated, depending on the patient's type of response (e.g. remission, good, moderate or no response, measured by the American College of Rheumatology (ACR) response criteria or by the disease activity score 28 (DAS28)). Furthermore, they assume a long-term deterioration in the HAQ score and a rebound effect when the treatment stops, i.e. for example a complete loss of the initial